

# Close Relationship between Carotid Intima-Media Thickness with Left Ventricular Hypertrophy in End-Stage Renal Disease Patients Undergoing Hemodialysis

Hamid Nasri, MD, Azar Baradaran, MD,\* and Forouzan Ganji, MD\*\*

## Abstract

**Background-** Two principal findings of cardiovascular disease in end-stage renal disease patients undergoing regular hemodialysis are left ventricular hypertrophy (LVH) and arterial disease due to rapidly progressive atherosclerotic vascular disease that can be characterized by an enlargement and hypertrophy of arteries (intima-media complex thickening, IMT). In this study, we sought to study the relationship between left ventricular hypertrophy with intima-media complex thickening in end-stage renal disease patients undergoing regular hemodialysis.

**Methods-** Sixty-one unselected patients with end-stage renal disease (ESRD) who were undergoing regular and maintenance hemodialysis treatment (F=23, M=38) were studied. The subjects consisted of 50 non-diabetic hemodialysis patients (F=20, M=30) and 11 diabetic hemodialysis patients (F=3, M=8). For all the subjects, echocardiography and carotid intima-media thickness measuring by B-mode ultrasonography were performed.

**Results-** In this study, there was a positive correlation between stages of LVH with duration of hemodialysis treatment, stages of hypertension (HTN), and with carotid-IMT. A positive correlation was also seen between stages of LVH and presence of chest pain, and more thickening of the intima-media complex was seen in the diabetic group. Diabetes mellitus was associated with the presence of chest pain, as was positive correlation between stages of HTN with IMT, and a reverse correlation was observed between IMT with the percent of cardiac ejection fraction.

**Conclusion-** Prevalence of thickening in intima-media complex is more evident in hemodialysis subjects with LVH. When there is LVH, IMT is similar in severity to the LVH (*Iranian Heart Journal 2006; 7 (1): 40-46*).

**Key words:** intima-media thickness Æ hemodialysis Æ left ventricular hypertrophy Æ atherosclerosis Æ diabetes mellitus

Cardiovascular disease is the principal cause of morbidity and mortality in dialysis patients.<sup>1</sup>

The principal findings of cardiovascular disease are left ventricular hypertrophy (LVH), as determined

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From the Department of Internal Medicine, Hajar Medical, Educational and Therapeutic Center, Shahrekord University of Medical Sciences, Section of Hemodialysis, Shahrekord, Iran, \* Department of Biochemistry, Center of Research and Reference Laboratory of Iran, Bu-Ali Hospital, Damavand St., Tehran, Iran and \*\* Postal Specialist in Community Medicine, Research Deputy, Shahrekord University of Medical Sciences, Varzesh St., Shahrekord, Iran.

Address correspondence to: H. Nasri, MD, Assistant Professor of Nephrology, Department of Internal Medicine, Hajar Medical, Educational and Therapeutic Center, Shahrekord University of Medical Sciences, Section of Hemodialysis, Shahrekord, Iran,  
Tel: 0098 911 2439584 Email: hamidnasri @ Yahoo. Com Fax: 0098 381 2243715 (hospital)

by echocardiography,<sup>2</sup> and arterial disease due to rapidly progressive atherosclerotic vascular disease<sup>3</sup>, characterized by an enlargement and hypertrophy of arteries (intima-media complex thickening), as can be determined by B-mode ultrasonography.<sup>2,3</sup>

LV mass increases progressively as renal function deteriorates and is exceedingly frequent in patients undergoing dialysis.<sup>4</sup>

In fact, left ventricular hypertrophy and arterial disease are the two principal risk factors for cardiovascular mortality in hemodialysis patients.<sup>5</sup> Carotid intima-media thickness (IMT) is a marker of early atherosclerosis, its anatomic extent and progression, and IMT is increased in subjects with several risk factors and is a predictor of cardiovascular events and end-organ damage.<sup>6</sup> Clinical manifestations of cardiovascular disease often arise in a stage of well-advanced atherosclerosis. However, arterial vessel wall changes occur during a presumably long sub-clinical lag phase characterized by functional disturbances and by gradual thickening of intima-media.<sup>6</sup> IMT of large peripheral arteries, especially the carotid, can be assessed by B-mode ultrasound in a relatively simple way, thus the measurement of IMT has emerged as one of the methods of choice for determining early atherosclerotic changes, the anatomic extent of atherosclerosis and its progression<sup>6</sup> and showing the effectiveness of medical therapy.<sup>6-8</sup> Therefore, considerable attention has been directed toward carotid-IMT by B-mode ultrasound, which can directly assess the IMT, corresponding to the thickness of the histologic intima and media.<sup>6-10</sup> Bodies of evidence have shown that carotid-IMT is a strong predictor of cardiovascular disease in the general population.<sup>6</sup> However, the question remains as to whether ultrasonographic studies of carotid arteries for IMT are useful to find any relationship between ESRD-related vascular changes

(IMT) with left ventricular hypertrophy and chest pain in hemodialysis patients. The cardiovascular mortality rate is elevated in those with end-stage renal disease (ESRD), diabetes mellitus and especially in those with diabetes mellitus and ESRD.<sup>10</sup> Therefore, we studied a group of hemodialysis patients consisting of diabetics and non-diabetics to find an association between IMT with LVH and IMT with severity of hypertension and chest pain.

## Patients and Methods

This cross-sectional study was done on 61 unselected patients with end-stage renal disease (ESRD), undergoing regular and maintenance hemodialysis treatment between September 2002 and December 2003. Patient exclusion criteria were cigarette smoking, body mass index (BMI) more than 25, anti-lipid drug use, recent MI and vascular diseases as well as pericarditis and pericardial effusion in echocardiography. For stratification of hypertensive patients, according to the sixth and seventh report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure, we stratified hypertensive patients from stage one to three<sup>11,12</sup> (stage zero equal to no HTN). Stages of hypertension of HD patients were considered before treatment and at the start of hemodialysis treatment; carotid sonography was done by a single sonologist unaware of history or lab data of patients with a Honda-HS-2000 Sonograph and 7.5 MHz linear probe to measure IMT. The procedure was done at the end of diastolic phase; the sites of measurements were at the distal common carotid artery, area of bifurcation and at the proximal internal carotid artery. IMT was measured at the plaque-free areas with subjects in the supine position with neck hyperextension and head rotation for

facilitation of the procedure. The carotids were evaluated in the longitudinal axis. By sonography, the carotid artery was found to have three different echoes: intima, as an echogenic layer line; media, as a hypo-echo layer; and an echogenic adventitia. Intima-media thickness (IMT) was defined as the distance from the leading edge of lumen-intima interface of the far wall to the leading edge of the media-adventitia interface of the far wall. IMT more than 0.8 mm was considered abnormal.

A single cardiologist unaware of the patients' data performed all the echocardiographies to determine left ventricular hypertrophy. On the basis of septal thickness, we stratified the patients to no LVH (septal thickness between 6-11 mm), mild (septal thickness between 11-15 mm), moderate (septal thickness between 15-18mm) and severe LVH (septal thickness >18mm). LVH measurements were done at the end-diastolic phase. Cardiac ejection fraction between 55 to 75% was considered normal. We measured the mean right and left carotid IMT. For statistical analysis, descriptive data are expressed as Mean±SD; comparison between groups was performed by using chi-square ( $\chi^2$  test), Mann-Whitney, as well as Kruskal-Wallis and Fisher's exact test. For correlations we used Spearman analytic test, and Phi and Cramer's V test and Eta test for partial correlations with adjustment for age. All statistical analyses were performed using SPSS version 11.00; statistical significance was inferred at a p-value< 0.05.

## Results

The total number of patients was 61 (F=23 M=38), which consisted of 50 non-diabetic hemodialysis patients (F=20, M=30) and 11 diabetic hemodialysis patients (F=3 M=8). Table I shows the mean ± SD of data; Tables II, III and IV show the

frequency distribution of chest pain, stages of HTN and stages of LVH in the patients. Mean ± SD of the age of the subjects was 46.5±16 years.

**Table I: Mean±SD, minimum and maximum of data.**

		Age years	D.H.T* months	IMT** mm	EF*** percent
total patients n=61	Mean±SD	46.5±16	32±31	1.06±0.3	51±8.9
	Min	15	2	0.50	25
	Max	78	108	1.70	70
diabetic n=11	Mean±SD	57±16	22.6±22	1.3±0.3	47.7±7
	Min	27	3	0.80	30
	Max	78	60	1.70	55
non-diabetic n=50	Mean±SD	47.8±16	34±33	1±0.25	51±9
	Min	15	2	0.50	25
	Max	78	108	1.60	70

\*duration of hemodialysis treatment, \*\*carotid intima-media thickness, \*\*\*cardiac ejection fraction

**Table II: Frequency distribution of stages of hypertension (HTN).**

Stages of HTN	Total patients n=61		DM group* n=11		Non-DM group n=50	
	No.	%	No.	%	No.	%
0	4	6.6	0	0	4	8
1	5	8.2	0	0	5	10
2	33	54.1	8	72.7	25	50
3	19	31.1	3	27.3	16	32

\*DM=diabetes mellitus

**Table III: Frequency distribution of chest pain in hemodialysis patients.**

Chest pain	Total patients n=61		Diabetic n=11	Non-diabetic n=50
	Number	Percent	Number	Percent
Yes	24	39.3	9	81.8
No	34	60.7	2	18.2

**Table IV: Frequency distribution of left ventricular hypertrophy (LVH) in hemodialysis patients.**

	Total patients n=61		Diabetic n=11	Non-diabetic n=50	
	Number	Percent	Number	Percent	Number
No LVH	9	14.8	1	9	8
Mild LVH	25	41	4	36.4	21
Mod. LVH	20	32.8	4	36.4	16
Severe LVH	7	11.5	2	18.2	5

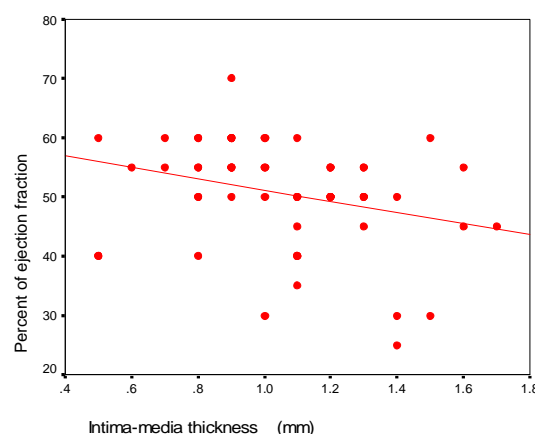
Mean±SD length of time the patients had been on hemodialysis was 32±31 months. Mean±SD cardiac ejection fraction was 51±8.9 percent, and 39.3% of the patients

had chest pain. In this study, there were no significant difference in age, percent of cardiac ejection fraction, IMT and duration of hemodialysis between the males and females ( $p>0.05$ , Mann-Whitney U test). Also, there was no significant difference in LVH between the two sexes ( $x^2$  test,  $p>0.05$ ).

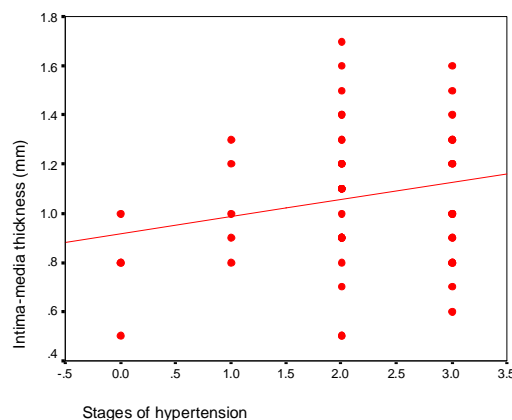
There was no significant difference in the presence of chest pain or DM between the two sexes (Fishers' exact test,  $p>0.05$ ). No significant difference was found between gender and stages of hypertension ( $p>0.05$ ,  $x^2$  test). In this study, there was a positive association between stages of LVH and duration of hemodialysis treatment ( $p<0.01$ ), and no significant difference between stages of LVH and age ( $p>0.005$ , Kruskal-Wallis) was found. There was a positive close relationship between stages of LVH and stages of HTN ( $r=0.580$ ,  $p<0.001$ ), but no significant correlation between DM and LVH ( $p>0.05$ , Phi and Cramer's V test). We found a significant difference between stages of LVH with carotid-IMT ( $p>0.05$ , Kruskal-Wallis test). We found a significant positive correlation between presence of chest pain and DM ( $p<0.001$ ), but no association between the presence of DM with presence of HTN, or gender with DM ( $p>0.005$ , Phi and Cramer's V test). There was a significant difference of carotid-IMT between the diabetic and non-diabetic groups ( $1.3\pm0.3$  vs.  $1\pm0.25$ mm, respectively,  $p<0.05$ , Eta test). No correlation was found between DM and ejection fraction ( $p>0.005$ , Eta test), and no significant difference existed between duration of hemodialysis, age and ejection fraction between the diabetic and non-diabetic groups ( $p>0.05$ , Mann-Whitney test).

No significant correlation was found between ejection fraction and duration of hemodialysis treatment ( $p>0.05$ , Spearman test). A significant correlation was observed between presence of chest pain and stages of LVH ( $p<0.001$ , Phi and

Cramer's V test). There was no difference between stages of HTN with presence of chest pain ( $p>0.05$ ,  $x^2$  test). Statistical analysis on IMT with partial correlation test after adjustment for age showed no positive correlation between IMT with duration of hemodialysis ( $p>0.05$ ), and reverse correlation between IMT with percent of ejection fraction ( $r = -0.353$ ,  $p=0.005$ , Fig. 1). Also, a positive association was observed between IMT and stages of HTN ( $r = 0.266$ ,  $p=0.020$ , Fig. 2).



**Fig. 1:** Reverse correlation between IMT with percent of cardiac ejection fraction ( $r= -0.353$ ,  $p=0.005$ , partial correlation test after adjustment for age).



**Fig. 2:** Positive correlation between IMT and stages of HTN ( $r = 0.266$ ,  $p=0.020$ , partial correlation test after adjustment for age).

## Discussion

The principal findings of the present study were a positive correlation between stages of LVH with duration of hemodialysis treatment; positive correlation between stages of LVH with stages of hypertension; significant differences between stages of LVH with carotid-IMT; and also a positive correlation between stages of LVH with presence of chest pain; more thickening of the intima-media complex in the diabetic group; and association of diabetes mellitus with the presence of chest pain as well as a positive correlation between stages of HTN with IMT, and reverse correlation between IMT with percent of cardiac ejection fraction. Strauman et al. in a study on 62 patients on maintenance hemodialysis observed 65% prevalence of LV hypertrophy and showed that age, body mass index and duration of HTN were associated with LV hypertrophy and asymmetric septal hypertrophy.<sup>13</sup> Greaves et al. in the evaluation of 30 HD patients and 54 patients under peritoneal dialysis compared with 38 ESRD patients not yet on dialysis demonstrated that left ventricular wall thickness was greater in the dialysis group.<sup>14</sup> De Lima et al. in their study of 103 HD patients showed that systolic blood pressure was significantly associated with LV mass and was significantly and independently correlated with LVH and posterior wall hypertrophy.<sup>15</sup> Nishizawa et al. in a study on 438 patients with ESRD treated with hemodialysis showed a significantly greater risk for death from cardiovascular causes in patients who had significant higher IMT.<sup>16</sup> Papagianni et al. in a study on 12 HD patients found a significant relationship between IMT and systolic blood pressure.<sup>8</sup> Lin et al. in a research on forty normotensive HD patients demonstrated that LV mass was significantly positively related to carotid-IMT.<sup>17</sup> London et al. studied 70

uncomplicated ESRD patients and observed a significant correlation of ventricular wall thickness as well as left ventricular mass with carotid-IMT.<sup>18</sup> Zoccali et al. in an evaluation of 254 patients undergoing dialysis concluded that LV mass is a strong and independent predictor of survival and cardiovascular events in these patients.<sup>4</sup>

Muiesan et al. in a study to evaluate the structural association between the carotid artery and left ventricle in a general population in northern Italy showed that the common carotid-IMT was significantly greater in subjects with concentric left ventricular hypertrophy.<sup>19</sup> Our results provide the first direct evidence that diabetic patients with ESRD undergoing hemodialysis treatment had more accelerated atherosclerosis and more involvement by ischemic heart disease (IHD) than non-diabetic hemodialysis patients. We were able to show the association between carotid-IMT and LVH and especially reverse correlation between IMT with cardiac ejection fraction, meaning that thickening of the intima-media complex and cardiovascular involvement, especially LVH in hemodialysis patients, could have an accelerated atherosclerotic base, albeit other factors are involved. We have also demonstrated that carotid artery-IMT is related to LVH, although the confirmation of this cardio-arterial interaction further highlights the importance of structural changes in large arteries in the pathogenesis of LVH in hemodialysis patients. Mallion<sup>20</sup> believed that the prevalence of thickening in intima-media was more evident in subjects with LVH and that the presence of concentric remodeling of the left ventricle without LVH was associated with an increase in IMT. He also believed that when there is LVH-in particular concentric-this IMT is similar in severity to the LVH, but the question is whether carotid

ultrasonography added relevant information to echocardiography-measured LVH in hemodialysis patients. Although IMT has a prediction power for cardiovascular death independent of LVH, larger studies are needed to allow of better appreciation of the relative value of ultrasonography-measured IMT in these patients.

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